

# MLPA Update

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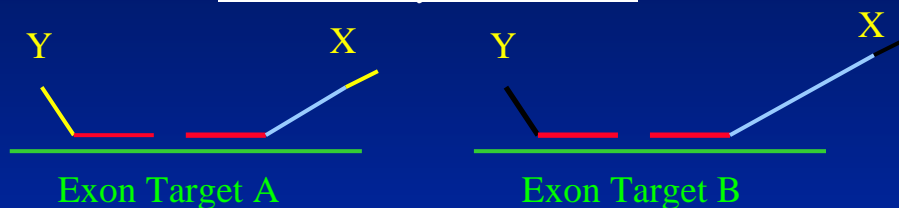
Stephen Thibodeau



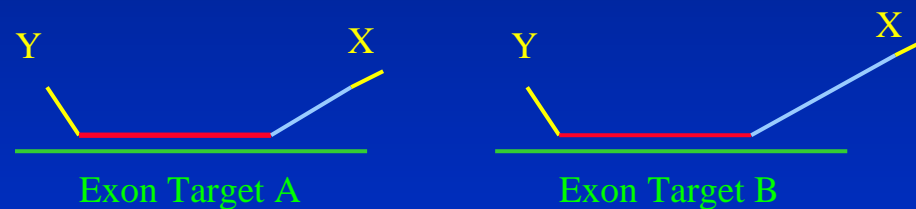
# hMSH2 / hMLH1

## *Multiple Ligation-Dependent Probe Amplification (MLPA)*

### 1. Probe Hybridization



### 2. Probe Ligation



### 3. Amplification and separation



Each exon probe product has  
unique length of 140-480 nt

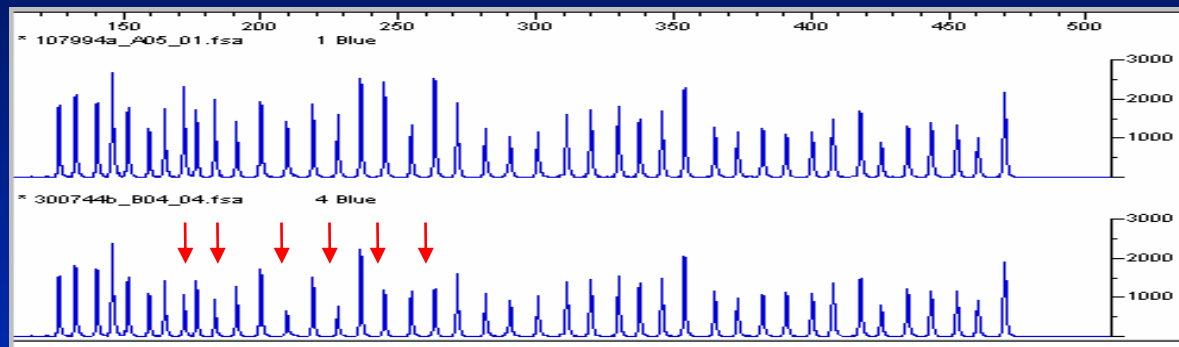
Gille et al, BJC, 2002



# hMSH2

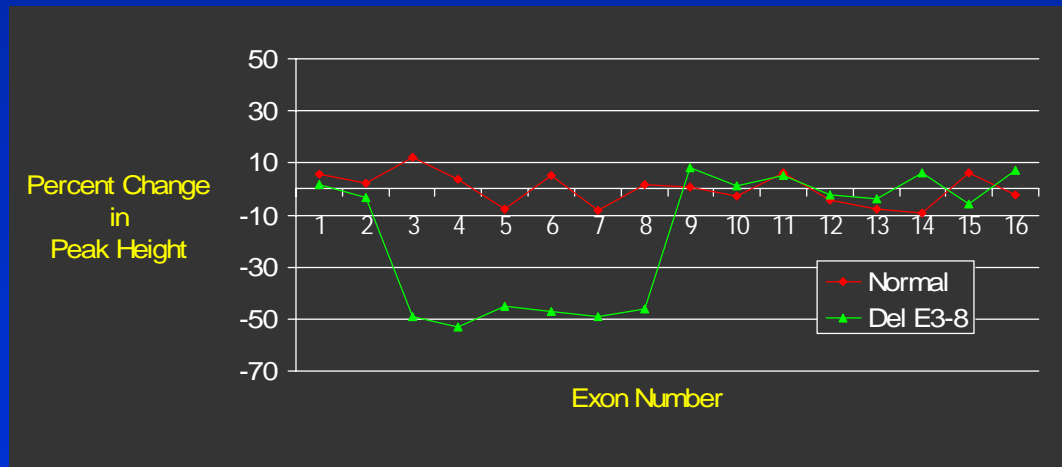
## MLPA (ABI 3100)

Exon: 3 4 5 6 7 8



Normal

Del E3-8



# MLPA Data Summary

- 1747 samples tested
- 46 positive samples (2.6%)
  - 45 deletions
  - 1 duplication
- 7 *hMLH1* deletions
- 38 *hMSH2* deletions
- 1 *hMSH2* duplication
- 25 failed

# MLPA Data Summary

Site	Negative	Deletion	Duplication	Pending / Equivocals	Failures	Total
Australia	275	18 (6.1%)	1	8	15	317
Seattle	571	1 (0.2%)	0	1	1	574
Hawaii	35	2 (5.4%)	0	0	0	37
Mayo	234	3 (1.3%)	0	0	5	242
Toronto	330	15 (4.3%)	0	1	1	347
USC	219	6 (2.7%)	0	2	3	230
<b>Total</b>	<b>1664</b>	<b>45 (2.6%)</b>	<b>1</b>	<b>12</b>	<b>25</b>	<b>1747</b>



<i>hMSH2 (38)</i>		<i>hMLH1 (7)</i>	
Mutation	n	Mutation	n
Del 1	2	Del 1-6	1
Del 1-2	3	Del 1-13	1
Del 1-6	6	Del 1-13	1
Del 1-8	2	Del 2-6	1
Del 1-11	1	Del 3	1
Del 1-16	7	Del 5	1
Del 2-6	1	Del 16-19	1
Del 3	1		
Del 3-7	1		
Del 5	3		
Del 8	7		
Del 8-15	1		
Del 9-10	1		
Del 9-12	1		
Del 11-16	1		
Dup 11-16	1		

# Other Findings

- 5 (Del artifact) DNA sequence change: 21
- 6 (Del artifact) normal on MLPA repeat: 13
- 7 (Del artifact) Southern did not confirm deletion: 3
- 8 (Del artifact) Sequencing and/or Southern ND (neg based on other similar cases): 1
  
- 10 (Dup artifact) normal on MLPA repeat: 34
- 11 (Dup artifact) Southern did not confirm duplication: 2
- 12 (Dup artifact) Sequencing and/or Southern ND (neg based on other similar cases): 8
  
- 14 (Eq) single exon del by MLPA, Eq artifact; Southern could not be performed: 11
- 15 (Eq) Multiple exons del by single MLPA; not enough sample for follow-up: 2
- 16 (Eq) single exon dup by MLPA, Eq artifact; Southern could not be performed: 1

# Where are we at!!

- Need to test affected family members
  - Need information from each of the groups to id samples that have been sent.
- Incorporate MSI, IHC, and results of MLH1 and MSH2 sequence analysis
- Write paper